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Comparison of Dried Vaccine with Fresh Indian Buffalo-Calf Lymph in Revaccination against Smallpox*

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It was known that the liquid glycerinated buffalo-calf lymph issued for routine use in smallpox vaccination in Madras gave a high take rate in primary vaccination but that successful takes on revaccination amounted to less than 10%. In the course of studies on smallpox carried out in Madras, it was therefore decided to compare a potent freeze-dried English vaccine with the current Madras lymph by revaccinations carried out on persons admitted to the Madras Infectious Diseases Hospital for ailments other than smallpox. The take rate of the freeze-dried preparation in these tests was 63% as against 27% for the liquid preparation. It would seem that, in the conditions prevailing in Madras at the time of the tests, the local lymph is not sufficiently potent for successful revaccination or for maintaining the immunity of the population at a satisfactory level. The authors suggest that freeze-dried vaccine produced in embryonated eggs might be more effective and economical.

Although the position in regard to primary vaccination against smallpox seems to be satisfactory in Madras, as indicated by the success rate of primary vaccination in young children, the position of successful revaccination is much less satisfactory. According to the reports of vaccinators the success rate on revaccination is less than 10%. This result is achieved with liquid glycerinated buffalo-calf lymph which must be used within seven days of issue. In view of these findings it was decided to compare a sample of freeze-dried vaccine prepared in England with the local vaccine prepared in Madras. The following observations are based on comparative studies made with these two "lymphs".

The dried preparation was made up with the diluting fluid supplied with the dried lymph immediately before use. The local Indian lymph was kept in a refrigerator from the time of issue until its use on the same subjects as were vaccinated with the reconstituted dried English preparation.

METHODS

Three separate trials were made, all on non-smallpox admissions to the Madras Infectious Diseases Hospital; all were revaccinations:

1. English lymph on both arms (50 revaccinations);

2. English lymph on right arm and Indian lymph on left arm (55 revaccinations);

3. English lymph on left arm and Indian lymph on right arm (23 revaccinations).

Revaccinations in Madras are normally performed on the left forearm. When English and

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Indian lymphs were compared, therefore, it was thought desirable to conduct two separate trials, alternating the lymph in relation to the arm, in order to avoid the effect of any possible local skin immunity on the left arm following earlier revaccinations. All vaccinations were performed with the rotary vaccinator commonly used in Madras, and were inspected after three days. Where results were completely negative a further inspection was made after five days. In some instances, the patient had been discharged or had left without permission before inspection was possible; these have been excluded from the series.

RESULTS

English lymph on both arms

Altogether 50 persons were vaccinated, but 4 remained untraced.

Of those examined (46), 24 had takes on both arms; 6 had takes on the left arm only; 8 had takes on the right arm only; 8 showed no reaction.

The percentage of over-all takes was therefore $\frac{38}{46} \times 100$, or 83%.

English lymph on right arm and Indian lymph on left arm

In this series, 55 persons were vaccinated, but 10 remained untraced.

Of those examined (45), 9 had takes on both arms; 2 had takes on the left arm only (Indian); 20 had takes on the right arm only (English); 14 had no reaction.

The percentage of takes with Indian lymph was therefore $\frac{9+2}{34} \times 100$, or 24%, and the percentage with English lymph was $\frac{9+20}{45} \times 100$, or 64%.

English lymph on left arm and Indian lymph on right arm

A total of 23 persons was vaccinated, but 2 remained untraced.

Of those examined (21), 6 had takes on both arms; 7 had takes on the left arm only (English), 1 had a take on the right arm only (Indian); 7 showed no reaction.

The percentage of takes with Indian lymph was therefore $\frac{6+1}{21} \times 100$, or 33%; and the percentage with English lymph was $\frac{6+7}{21} \times 100$, or 62%.

Summary

The foregoing figures may be summarized as follows:

1. Where English lymph was used alone on both arms the take rate (46 revaccinations) was 83%.

2. Where Indian and English lymphs were compared by vaccinating the same person with a different lymph in each arm, the following percentages of takes were found (second and third tests combined):

Indian: $\frac{18}{66} \times 100$, or 27%;

English: $\frac{42}{66} \times 100$, or 64%.

An examination of these figures shows that the difference between the proportions is nearly five times the standard error, and that the over-all differences in results between Indian and English lymph are therefore very significant. The use of Indian lymph on left and right arms separately gave take rates of 24% and 33% respectively. This difference, statistically, is within the limits of reasonable chance. The difference between the proportions is less than two times the standard error. The normal success rate for revaccinations in Madras, as quoted in the report of the Corporation Health Officer, is 7.5%.

DISCUSSION

The results in these comparative tests on a limited number of subjects give a higher take rate on revaccination with the Indian lymph than that reported by the public vaccinators. This is probably due to the fact that in the comparative tests reported above the Indian lymph was kept at the Infectious Diseases Hospital in the refrigerator at about 4° C until the time of use, whereas the lymph used for revaccination usually issued to the public vaccinators is kept for a period of up to seven days, perhaps not always at a suitable storage temperature.

The success rate with the dried English preparation was rather lower than that found with the same preparation of Royal Air Force recruits in the United Kingdom, among whom the success rate on revaccination was of the order of 90%. However, the chances of previous undetected revaccination were much greater in Madras than among service recruits in the United Kingdom, and this alone would tend to lower the apparent success rate. The lower rate in the Madras trials may also have been due to the fact that some of

the patients were not seen after the third or fourth day because they left the hospital. It is possible that a few of the subjects who were sufficiently susceptible to have given a primary type of take might have been negative on the third day and positive on the fourth or fifth day when they were no longer available for inspection. This consideration obviously applies to the same subjects who were vaccinated also with the Indian lymph. Therefore, the success rate given above in the comparative tests is probably a little lower than it might have been if inspection had been possible on the third day and sometimes the fifth day, or, indeed, if all persons had been available on the fifth, sixth or seventh days after revaccination.

The Indian lymph was prepared at the King Institute, Guindy, Madras, and gives nearly 100% takes on primary vaccination. It is obviously a satisfactory product for primary vaccination. For revaccinations, however, it seems that its potency was not sufficiently high to give the high percentage of takes desirable, the dried preparation giving a success rate approximately 2½ times that of the liquid preparation. The lymph prepared is of good quality, but is diluted in order to meet the enormous demands of the population to be served.

It seems, therefore, that under the conditions prevailing in Madras and the surrounding area—among them the varying temperatures and lack of storage facilities, particularly in the outlying villages—liquid vaccine is not the solution to India's vaccination problems. A freeze-dried preparation which would be less dependent on low-temperature storage and which would remain potent for a very much longer time would in the long run be much more effective and more economical than the liquid product.

In India buffalo-calf lymph is used at the present time. An alternative source of vaccinia virus worthy of serious consideration would be embryonated eggs. Production of a potent vaccine can be carried out easily and relatively inexpensively with eggs and will give a final product which is bacteriologically sterile. Moreover, production can continue uninterruptedly throughout the year in amounts which should easily meet all possible local demands for smallpox vaccine. On the other hand, vaccine prepared in liquid form from buffalo calves yields a product which is never bacteriologically sterile and usually has to be kept some months with 50% glycerol until the bacterial count is reduced to one which meets minimum requirements in this respect. Furthermore, the local cattle are apt to suffer periodically from outbreaks of foot-and-mouth disease. Such outbreaks often hold up production of lymph for months at a time and make it impossible to have continuous production of lymph sufficient for local needs. At the present time, when a world-wide smallpox eradication programme is under way, it seems important to produce the best possible vaccine to ensure that all the money and the labour of so many workers to fulfil this programme are not to be in vain.

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RÉSUMÉ

On savait que la lymphe glycérinée préparée sur le buffle pour vacciner couramment contre la variole, à Madras, donnait un taux élevé de primovaccinations positives, mais que ce taux n'était que de 10% environ lors des revaccinations.

Dans le cadre des études sur la variole entreprises à Madras, la lymphe de buffle liquide a été comparée à la lymphe desséchée, de provenance anglaise, sur 46 jeunes malades, admis à l'hôpital pour des causes autres que la variole. Le taux de « prises » a été de 63% pour le vaccin sec (reconstitué au moment de l'emploi) et de 27% pour la lymphe de buffle conservée au réfrigérateur. Ces résultats indiquent que la préparation liquide d'origine locale n'est pas assez active pour assurer le succès des revaccinations et, par conséquent, pour maintenir à un niveau suffisant l'immunité générale de la population. Les auteurs proposent qu'un vaccin sec, préparé sur œuf embryonné, soit essayé, étant plus efficace et moins coûteux.